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THE DIFFERENTIATION AND DISTRIBUTION OF THE PARATYPHOID-ENTERITIDIS GROUP

V. OCCURRENCE IN THE HUMAN INTESTINE

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Many investigators, particularly in Germany, have reported finding bacilli belonging to the paratyphoid-enteritidis group widely distributed in nature: in water, ice, milk, chopped meat, sausage, in the healthy organs of normal food animals, in the intestinal contents of various healthy domestic animals and of man, in the dejecta of typhoid carriers and convalescents and of persons ill with other diseases.[1]

Other investigators have not been able to confirm these statements of the "ubiquity" of paratyphoid organisms.[2]

Poppe[3] has given a summary and full bibliography of the observations on the occurrence of the paratyphoid group in foodstuffs and in the organs and intestinal contents of domestic animals, and concludes that the assumption of a widespread distribution is hardly justified by the facts.

There are, of course, many instances on record in which paratyphoid bacilli have been found in the stools of patients supposed to be suffering from typhoid fever, but in most instances of this sort the diagnosis of typhoid has been pronounced either on clinical grounds or on the results of an agglutinative test. Neither method gives assurance that the typhoid bacillus was really the infecting agent; as is well known the clinical symptoms of paratyphoid infection are sometimes such that they cannot be distinguished from those produced by the typhoid bacillus, and the agglutinative reactions of the patient's blood have likewise been shown to be confusing and not fully differentiative.

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[1] Conradi: Deutsch. med. Wchnschr., 1904, 30, p. 1165. Nieter: München. med. Wchnschr., 1907, 54, p. 1622. Mühlens, Dahm and Fürst: Centralbl. f. Bakteriol., I, O., 1908-1909, 48, p. 1. Conradi: Klin. Jahrb., 1909, 21, p. 421. Rommeler: Deutsch. med. Wchnschr., 1909, 35, p. 886; Centralbl. f. Bakteriol., 1909, I, O., 50, p. 501. G. Mayer: Centralbl. f. Bakteriol., 1909-1910, I, O., 53, p. 234. Komma: Centralbl. f. Bakteriol., 1910, I, O., 55, p. 1. Hübener: Fleischvergiftungen und Paratyphusinfektionen, 1910, p. 66.

[2] Trautmann: Ztschr. f. Hyg. u. Infectionskrankh., 1906, 54, p. 104. Mayer, O.: Klin. Jahrb., 1909, 21, p. 325. Bainbridge and O'Brien: Brit. Med. Jour., 1910, II, p. 1503. Aumann: Centralbl. f. Bakteriol., 1910-11, I, O., 57, p. 310. Zweifel: Centralbl. f. Bakteriol., 1911, I, O., 58, p. 115. Horn and Huber: Ztschr. f. Inf. d. Haustiere, 1911, 10, p. 443. Clausnizer: Arch. f. Hyg., 1913, 80, p. 1.

[3] Arch. f. Hyg., 1913, 80, p. 216.

Eliminating such instances, as well as those of healthy carriers known to have had paratyphoid fever or to have been in contact with cases, there remain a number of instances in which paratyphoid bacilli have been reported as found in the stools of patients who have had genuine typhoid fever.[4]

A certain proportion of such cases are doubtless to be regarded as mixed infections and do not come properly within the scope of this inquiry. The questions that seem to need consideration are (1) how far the frequency of occurrence of paratyphoid bacilli in typhoid stools indicates that secondary infection with these organisms is common, and (2) whether paratyphoid bacilli are as frequently present in normal and diseased human intestines as maintained by some German observers.

One of us has previously put on record a series of observations on the intestinal contents of healthy swine killed in the Chicago stockyards.[5] The results (291 animals) were negative; not a single organism was found that could be identified as belonging to the true B. suipestifer type. The present paper deals with examinations of the feces of typhoid patients and convalescents and of patients suffering from other diseases.

Forty carefully selected cases of active typhoid were examined, mainly in the 2nd to the 4th week of the disease, altho in several instances examinations were made up to the 8th week and later. The total number of feces examinations was 77, the number for an individual ranging from 1-6 depending on the stage of the disease and the character of the findings. B. typhosus was isolated from the blood of 11 of these cases and from the stools of 7 (both blood and stools, 3); in 9 other cases the agglutination was positive; in the remainder (17) no blood examination was made and no agglutination test recorded on the hospital records. Thirteen of the cases occurred during a single water-borne epidemic in a small city when hospital and laboratory facilities were for the time overtaxed. There is no reasonable doubt that all the 40 cases were genuine typhoid.

The Endo medium was used throughout the series of fecal examinations; in many of the cases brilliant green medium, which is especially favorable for paratyphoid bacillus isolation, was used to supplement the former. China green was also used in a few cases. The applicability of the methods used was shown by the ease with which paratyphoid bacilli could be isolated from the stools of a case of paratyphoid B infection previously described by us,[6] and also from a case of paratyphoid A infection clinically resembling mild typhoid and met with by us in the course of our study of active typhoid cases.

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[4] Gaehtgens: Arb. a. d. k. Gsndhtsamte, 1907, 25, p. 203. Marmann: Hyg. Rundsch., 1908, 18, p. 1013. Rimpau: Deutsch. med. Wchnschr., 1908, 34, p. 1045. Hübener: Centralbl. f. Bakteriol., 1909, I, Ref., 44, Supp. p. 136.

[5] Jordan: Jour. Infect. Dis., 1918, 22, p. 252.

[6] Jordan and Irons: Jour. Infect. Dis., 1915, 17, p. 234.

In all 649 colonies were picked. Thirty strains from 13 cases were characterized provisionally as paratyphoid-like, that is, dextrose +, lactose —, gelatin not liquefied. These were then subjected to further tests according to the system adopted in an earlier paper.[5]

The following examinations have been made of the stools of typhoid convalescents: 38 men — students in the University of Chicago — who had a definite history of typhoid as follows: in twelve the attack was 12-19 years before the examination; in seventeen, 4-11 years; in eight, less than 3 years and in one, unknown. A single examination by the Endo plate method was made in each case. In all 326 colonies were picked. B. typhosus was not found in any case, nor were any bacilli of the paratyphoid group present. In nearly all instances B. coli and streptococci were the only organisms found. No paratyphoid-like organisms were found. The flora in these healthy convalescents was much less varied than that observed in active cases of typhoid.

Forty-nine women — University of Chicago students — with a definite history of typhoid as follows: in fifteen the attack was 12-25 years before the examination; in twenty-seven, 4-11; in four, less than 3 years and in three, unknown. Four hundred and eight colonies were picked by the Endo plate method, a single examination being made in each case. Bacillus typhosus was not found and the flora was composed mainly of B. coli and streptococci as in the 38 cases just described. Bacilli with paratyphoid-like characters were found in 4 cases. In one of these (Case 156) a second examination after an interval of 6 weeks showed the same organism present. The typhoid attack in this individual had occurred 7 years previously. Several strains of this organism proved identical. On subjecting this bacillus to further tests, it was found to differ in several cultural reactions from the true paratyphoid group, and it did not agglutinate with paratyphoid or enteritidis sera in high dilutions. In the 3 other cases also (Cases 104, 120, 140) in which paratyphoid-like organisms were found the bacilli in no instance agreed in all their cultural characters with true paratyphoid B bacilli and did not agglutinate with B. paratyphosus B and B. enteritidis serums.

The stools in 11 cases of disease other than typhoid were examined. These comprised 3 cases of enteritis, 1 case of carcinoma, 1 of pleurisy, 1 of lobar pneumonia, 2 of ulcerative colitis, 1 of dysentery (neither dysentery nor typhoid bacilli were found) and 2 of an intestinal affection of obscure nature. The same method of plating was used as just described and 156 colonies were picked from the plates made from stools of these patients; on further examination but 2 of these were paratyphoid-like (Cases 52 and 71). One of these strains produced indol and failed to ferment rhamnose or sorbit. The other produced indol and fermented salicin. The intestinal flora disclosed by the mediums used did not differ appreciably from that observed in the typhoid cases: B. pyocyaneus was very abundant in 1 stool and B. fecalis in another; 3 had large numbers of streptococci.

The characters of the paratyphoid-like cultures isolated in these 3 series are shown in Table 1.

SUMMARY AND DISCUSSION

In this series of cases nothing has been found that supports the assumption of a common or widespread distribution of paratyphoid bacilli apart from their association with specific disease conditions. It is true that bacilli with some of the more salient characteristics of

TABLE 1

Cultural Characters of Paratyphoid-like Bacilli from Human Intestines

Active Typhoid Cases

Case No.	No. of Strains	Paratyphosus B Typical Reaction in Milk	Indol	Salicin	Sorbit	Rhamnose	Remarks
4	1	—	—	+	—	+	Culturally very close to paratyphosus B (but indol +). No trace of agglutination with 1:100 paratyphosus B and enteritidis serums (5,000 titer)
5x	2	—	+	—	+	+	
5y	5	+	+	—	+	+	
24	7	+	+	—	—	—	
32x	5	—	+	—	—	+	
32y	2	+	—	—	—	+	
34x	7	—	+	—	—	+	
34y	3	—	—	—	—	—	
37	2	—	—	—	+	+	
41	1	+	+	+	+	+	
43	5	—	+	+			
45x	1	+	+	—	—	—	
45y	1	—	+	—	—	—	
				Old Typhoid History			
104♀	4	+	—	—	—	—	
120♀	1	—	—	+	—	+	Typhoid 7 years before
140♀	2	—	—	+	—	+	Typhoid 4 years before
156♀	2	+	+	+	+	+	Typhoid 7 years before. Two examinations at interval of 6 weeks yielded this organism together with B. coli
				Nontyphoidal Diseases			
52	1	+	+	—	—	—	Ulcerative colitis
71	2	+	+	+	+	+	Enteritis

In Table 2 the results are summarized.

TABLE 2

Results of Bacterial Feces Examination

Fecal Examinations in	No. of Cases	No. of Colonies Picked	No. Paratyphoid-like	No. True Paratyphoid
Active typhoid	40	675	42 (13 strains from 9 cases)	0
Healthy persons (old typhoid history)	87	734	9 (4 cases)	0
Nontyphoidal diseases	11	156	3 (2 cases)	0

paratyphoid bacilli have been found in normal and diseased human intestines, but these have invariably shown cultural deviation from the true paratyphoid type. Moreover, even those that resemble most closely paratyphoid bacilli in their cultural characters have failed to agglutinate with highly potent specific serums prepared from typical members of this group. No true paratyphoid bacilli have been found.

As seen in Table 1, paratyphoid-like organisms are isolated more frequently from the stools of active typhoid cases than from those of healthy persons who had had typhoid some years previously. The intestinal flora of the latter in fact does not differ appreciably from that of normal individuals not known to have had typhoid. It is worth noting that the 4 persons with old typhoid history in whose stools paratyphoid-like bacilli were found were all women (4 of 49 examined), while none of the men of the same series (38) harbored such organisms. The larger proportion of women than of men typhoid carriers is well known.

The 19 strains of bacilli denominated as paratyphoid-like (dextrose +, lactose—, gelatin not liquefied in this series have given paratyphoid-like reactions in other mediums as follows:

Milk	9
Indol	7
Salicin	11
Sorbit	6
Rhamnose	11

Combining these with similar tests made on 18 strains of paratyphoid-like organisms isolated from healthy swine intestines,[5] it appears as if the milk and indol reactions were better fitted for differentiating these organisms from the true paratyphoid bacilli than the fermentation results in salicin, sorbit and rhamnose. More than half of these bacilli (22 of 37) fail to ferment salicin, in this respect agreeing with true paratyphoid organisms, but only 14 of 37 give the paratyphoid reaction in milk and only 16 of 37 fail to produce indol.

It will be noticed (Table 1) that in a number of active typhoid cases different varieties of paratyphoid-like bacilli were found in the stools of one and the same individual (Cases 5, 32, 34, 45). This corresponds with the generally heterogeneous bacteriologic characters of such stools. It is evident that the bacterial flora of typhoid stools is more varied than that of normal stools. There is, however, no reason for assuming without further investigation that this condition is peculiar to the intestinal tract of typhoid patients. The few observations here recorded on the stools of persons suffering from other disorders, especially disorders of the alimentary tract, indicate that the proportion of bacterial abnormalities in such cases is probably not very different from that in typhoid cases.

The occurrence in typhoid stools of such paratyphoid-like bacilli, or, as some writers call them, paracolon bacilli, has been noted by several investigators.* Seiffert[7] has described 3 such strains. Fletcher[8] found in the stools of soldiers convalescent from diseases of the dysentery and enteric groups a number of organisms that he called "anomalous organisms of the Salmonella group." These were generally to be distinguished by their lack of motility or by their power to form indol. Extensive fermentation tests were not made. Agglutination reactions with paratyphoid sera were negative. Fletcher found such organisms at times "very common."

Agglutination tests have been made repeatedly with all the strains here mentioned. Rabbit serums have been used prepared with several strains of B. paratyphosus B, with 2 strains of B. paratyphosus A, 2 of B. suipestifer and 2 of B. enteritidis. These serums have agglutinated the homologous organisms in about 1:4,000 to 1:5,000 dilutions (in the case of B. enteritidis 1:20,000). In no instance have any of these culturally anomalous intestinal strains agglutinated in dilutions higher than 1:100. It has been exceptional indeed to observe even a trace of agglutination in a 1:100 dilution.

A serum prepared with one of these intestinal cultures, 32x (titer 1:1,000) did not agglutinate other intestinal strains and did not agglutinate 2 other strains isolated at the same time from the same cases and showing similar cultural characteristics. Serums were prepared with 2 other strains from other cases with precisely similar results. The titer reached with these 3 strains was not very high (1:1,000 to 1:2,000), but in no single instance was agglutination observed in 1:100 dilutions with any of the other intestinal strains here enumerated. This was true in the case of those strains showing close cultural resemblance as well as those showing considerable divergence. In this respect the behavior of these "paratyphoid-like" organisms is not very different from that of colon bacilli.

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* The term paracolon bacillus might well be restricted to such organisms as ferment lactose with or without gas production, but fail to give certain typical coli-like reactions such as indol production, altho in other respects closely related to the true B. coli. The term paratyphoid-like is awkward, but has some advantages when used to designate the nonlactose fermenters.

[7] Ztschr. f. Hyg. u. Infectionskrankh., 1909, 63, p. 273.

[8] Jour. Roy. Army Med. Corps, 1918, 30, p. 57.